

Serial No. 10/750,996
Docket No. SHE0065.00**In the Claims:**

Please cancel claims 38-65 without prejudice and with the ability to prosecute the canceled subject matter in one or more applications. This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Original) A method for preparing a polymer conjugate, said method comprising:

(a) providing a water-soluble polymer comprising a maleimide group,

(b) reacting said polymer with an active agent comprising a nucleophile under conditions effective to couple said agent to said water soluble polymer via a Michael-type addition reaction to form a polymer-succinimide-linked active agent conjugate, and

(c) treating the conjugate from (b) under conditions effective to force open said succinimide ring to thereby form a polymer-conjugate composition comprising a polymer-succinamic acid-conjugate.

2. (Original) The method of claim 1, wherein said treating step comprises hydrolysis.

3. (Original) The method of claim 2, wherein said treating is carried out in an aqueous or an organic solvent.

4. (Original) The method of claim 1, wherein said treating step is carried out in the presence of base.

5. (Original) The method of claim 4, wherein said base is selected from the group consisting of metal or non-metal hydroxides, quaternary ammonium hydroxide, sodium (Na⁺), and potassium (K⁺).

6. (Original) The method of claim 4, wherein said base is on a solid support or in solution.

Serial No. 10/750,996
Docket No. SHE0065.00

7. (Original) The method of claim 1, wherein said treating step is carried out at pHs ranging from about 6 to 12.
8. (Original) The method of claim 7, wherein said treating step is carried out at pHs ranging from about 7.5 to about 11.
9. (Original) The method of claim 1, wherein said treating step is carried out in a buffer.
10. (Original) The method of claim 1, wherein said treating is carried out under conditions effective to provide a chemically stable composition.
11. (Original) The method of claim 1, further comprising the step of determining the extent of opening of said succinimide ring in said composition.
12. (Original) The method of claim 11, wherein said treating is carried out until at least about 15% of the polymer-succinamic acid-conjugate is formed.
13. (Original) The method of claim 11, wherein said treating is carried out until at least about 35% of said polymer-succinamic acid-conjugate is formed.
14. (Original) The method of claim 11, wherein said treating is carried out until at least about 80% of said polymer-succinamic acid-conjugate is formed.
15. (Original) The method of claim 11, wherein said treating is carried out until at least about 95% of said polymer-succinamic acid-conjugate is formed.
16. (Original) The method of claim 11, wherein said treating is carried out until at least about 98% of said polymer-succinamic acid-conjugate is formed.
17. (Original) The method of claim 1, wherein said nucleophile is a sulfhydryl (thiol) group or an amino group.

Serial No. 10/750,996
Docket No. SHE0065.00

18. (Original) The method of claim 1, wherein said active agent is a protein or a peptide.
19. (Original) The method of claim 1, further comprising recovering said polymer succinamic acid conjugate from the composition.
20. (Original) The method of claim 19, wherein said recovering step comprises precipitating said polymer succinamic acid conjugate.
21. (Original) The method of claim 19, wherein said recovering step further comprises purifying said polymer succinamic acid conjugate.
22. (Original) The method of claim 21, wherein said purifying step comprises purifying said polymer succinamic acid conjugate by chromatography.
23. (Original) The method of claim 22, wherein said chromatography is selected from the group consisting of SDS-PAGE, gel permeation chromatography, and ion exchange chromatography.
24. (Original) The method of claim 1, wherein said water soluble polymer is selected from the group consisting of a poly(alkylene oxide), poly(vinyl pyrrolidone), poly(vinyl alcohol), polyoxazoline, poly(acryloylmorpholine), and poly(oxyethylated polyol).
25. (Original) The method of claim 24, wherein said water soluble polymer is a poly(alkylene oxide).
26. (Original) The method of claim 25, wherein said water soluble polymer is a poly(ethylene glycol).
27. (Original) The method of claim 26, wherein the poly(ethylene glycol) comprises an end-capping moiety.

Serial No. 10/750,996
Docket No. SHE0065.00

28. (Original) The method of claim 27, wherein the end-capping moiety is selected from the group consisting of alkoxy, substituted alkoxy, alkenyloxy, substituted alkenyloxy, alkynyloxy, substituted alkynyloxy, aryloxy, and substituted aryloxy.

29. (Original) The method of claim 28, wherein the end-capping moiety is selected from the group consisting of methoxy, ethoxy, and benzyloxy.

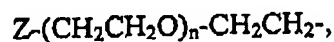
30. (Original) The method of claim 26, wherein the poly(ethylene glycol) has a nominal average molecular mass of from about 100 daltons to about 100,000 daltons.

31. (Original) The method of claim 30, wherein the poly(ethylene glycol) has a nominal average molecular mass of from about 1,000 daltons to about 80,000 daltons.

32. (Original) The method of claim 31, wherein the poly(ethylene glycol) has a nominal average molecular mass of from about 2,000 daltons to about 50,000 daltons.

33. (Original) The method of claim 26, wherein said poly(ethylene glycol) has a structure selected from the group consisting of linear, branched, forked, and multi-armed.

34. (Original) The polymer of claim 26, wherein said poly(ethylene glycol) comprises the structure:



where n is from about 10 to about 4000, and Z comprises a moiety selected from the group consisting of hydroxy, amino, ester, carbonate, aldehyde, aldehyde hydrate, acetal, ketone, ketone hydrate, ketal, alkenyl, acrylate, methacrylate, acrylamide, sulfone, thiol, carboxylic acid, isocyanate, isothiocyanate, hydrazide, urea, maleimide, vinylsulfone, dithiopyridine, vinylpyridine, iodoacetamide, alkoxy, benzyloxy, silane, lipid, phospholipid, biotin, and fluorescein.

Serial No. 10/750,996
Docket No. SHE0065.00

35. (Original) The method of claim 1, wherein said water-soluble polymer comprises a linker, L, interposed between said water-soluble polymer and said maleimide group.

36. (Original) The method of claim 35, wherein said linker is effective to result in a ring-opening hydrolysis half-life of said water-soluble polymer of about 12 hours or less when measured at room temperature in phosphate buffer at pH 9.0.

37. (Original) The method of claim 26, wherein said polyethylene glycol polymer is directly attached to the nitrogen atom of said maleimide group.

38-65. (Canceled).

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